Professor Joshua Lederberg
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Dear Professor Lederberg,

I must ask you first to excuse me for addressing you in such abrupt manner. I know that it is most impertinent to demand advice to someone who is not willing to give it,but as I am badly in need I trespassed this elementary rule and I am writing you.

I am a relatively young worker in the field of microbial variability.In the course of a work on recombination in Serratia marcescens I was put in the awkward situation to decide whether adaptation can coexist with mutation-selection in the teritory of drug resistance.The number of those who believe that drug resistance in bacteria is due to progressive adaptation is rather small.As you know they are crowded mainly in Cambridge,England,under the banner of Sir Cyril Hinshelwood and are waging a phony war to their over-there and over-here colleagues.They issued a book summing up their collective effort on adaptation in bacteria/Cambridge,1953/. Iread this book in an excellent russian translation and Ifound that there is something in it.I was thus obliged to decide in my mind,because indecision in our particular field leads to error and error to disaster.

I tried to devise an experimental system which would leave but little room for doubt.It was my desire to attack directly the problem as I did not want to prove the reality of mutation but to prove or disprove the existance of induction of antibiotic-resistance. In this scope I looked for your replica-plating method/J.Bact.1952,63,399/but as RYAN et al. showed/J.Bact.1955,69,552/resistant clones may spring on the top sensitive mother colonies I felt that the velveteen stamp could carry secondary clones and thus give a false argument to adaptation.Finally I choosed the antibiotic-gradient plate of BRYSON & SZYBALSKI /Science 1952,116, 45/ and the experiment was devised in the following manner: on a streptomycin-gradient plate /the highest concentration-1oo gamma/ I laid some cellophane triangles/grossly isoscels, catheta 1.5 cm long/. These triangles were laid on the drug-free zone of the plate and seeded with one cell of Serratia marcescens strain T/initial resitance to dihydrostreptomycin RAFFA:3.3 gamma per ml/. After the colony has developped/18 hrs at 22°C/the triangle was pulled gradually accross the plate to the antibiotic-full margin.This was done in five days. When the drug-full margin was reached,the triangles were removed from the plate and the colonies separated from their cellophane support by stirring in a 1o ml broth containing test tube.Adequate dilutions were made and plated for viable count and streptomycin-resistance.The results indicated that the vast majority of germs were killed by the gradual contact with the

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antibiotic and only ten or so cells escaped this fate /ten in a billion in the control/.It must be noted that these cells remained streptomycin-sensitive.

Now,why do I seek your advice? May I interpret these results as indicating that direct induction of antibiotic-resistance does not exist and all the brilliant ratiocinations of the cambridgians are but blah-blah-blah? Prior to the experiments I believed that my system will radically decide in the case mutation versus adaptation. There are already strong proofs accumulated against drug-adaptation,may I consider my experiments as such a proof?

I am most anxious to read your reply and begging you again to excuse me for my abrupteness I remain

Sincerely yours,

Eugene Isaac Altescu M.D.

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